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10/009,926	12/06/2001	Octavian Schatz	P1687USA	6712

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WOOD, PHILLIPS, KATZ, CLARK & MORTIMER
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CHICAGO, IL 60661

EXAMINER

SAKELARIS, SALLY A

ART UNIT PAPER NUMBER

1634

DATE MAILED: 07/25/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/009,926	SCHATZ, OCTAVIAN	
	Examiner	Art Unit	
	Sally A. Sakelaris	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 04 May 2005.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 21-34 is/are pending in the application.
- 4a) Of the above claim(s) 35 and 36 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 21-34 and 37 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some * c) ☐ None of:
1. ☒ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|---|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submissions filed on 5/4/2005 has been entered.

Claims 21-34 and 37 are pending, with claims 35 and 36 being withdrawn. Claims 21 and 25 have been amended. Applicant's amendments and arguments have been thoroughly reviewed, but are not persuasive for the reasons that follow. Any rejections not reiterated in this action have been withdrawn as necessitated by applicant's amendments to the claims. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

1. Claims 21-34 and 37 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

A. Claims 21-34 and 37 are rejected over the recitation of "cannot bind the matrix" in steps ab) and bb) of claim 21. It is not clear what, if any, structural limitations are being imposed on

Art Unit: 1634

the oligonucleotide that cause its inability to bind the matrix. Appropriate clarification is suggested.

Response to Arguments:

Applicant's arguments filed 5/4/2005 have been fully considered but they are not persuasive. Applicants submit that the passage on page 10 lines 1-13 of their specification clearly describes how the oligonucleotide recited in steps ab) and bb) cannot bind to the matrix. Applicant should note that limitations in applicant's arguments, specification etc couldn't be read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993). The passage provides only exemplary description of mechanisms by which oligonucleotides can be linked to a matrix , and is void of an explicit definition of ways in which the oligonucleotide "cannot bind to the matrix". Even if arguendo, the specification did teach a specific blocking agent, the limitation may not be read into the claim and furthermore even with a blocking agent, an oligonucleotide can be made to bind to the matrix via exposure to UV light and through the resulting cross-links. As such, the recitation of "cannot bind the matrix" is still considered indefinite. It is again suggested that applicant amend the claim to recite a specific structure had by the oligonucleotide that disallows it to bind the matrix.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

It should be noted that the art has been applied in view of the indefiniteness rejections made above and as best as the examiner can understand the invention being claimed.

2. Claims 21-27, 29-32, 34, and new claim 37 are rejected under 35 U.S.C. 103(a) as being unpatentable over DuBridge et al.(US Patent 5,888,737) in view of Church et al.(US Patent 6,485,944).

With regard to claim 1, DuBridge et al. teach a method for the production of a nucleic acid molecule comprising the steps

a) providing an oligonucleotide which is prepared by the following steps:

aa) coupling one end of an oligonucleotide to a solid matrix(Col.19 lines 1-60) wherein the coupling is effected by means of a modification such as highly crosslinked polystyrene beads providing bead-polynucleotide conjugates(Col. 19 lines 65-67 and Col. 20 line 3), and the polynucleotide contains a recognition sequence for a type IIS restriction enzyme(Col. 11 lines 28-37 for example) which cleaves outside its recognition sequence. The reference teaches that “prior to ligation, ends of polynucleotides to be analyzed are prepared by digesting them with one or more restriction endonucleases that produce predetermined cleavages, usually having 3’ or 5’ protruding strands”(Col. 6 lines 21-25).

ab) adding an additional oligonucleotide(Col. 13 and 14 any one of A1, A2, A3 or the “stepping adaptor” references)separate from the oligonucleotide of aa) which is at least partially double stranded(col. 3 line 26 for example) and contains a different recognition sequence than in step aa) for a type IIS restriction enzyme which cleaves outside its recognition sequence, whereby this oligonucleotide cannot bind the matrix, in their teaching of “many target polynucleotides in parallel” and “attaching a first oligonucleotide tag from a repertoire of tags to

Art Unit: 1634

each polynucleotide in a population of polynucleotides” and “further sampling the population of polynucleotides such that substantially all different polynucleotides in the population have different first oligonucleotide tags attached”(See Col. 11-12, and figures 2A-3E)

ac) ligating the oligonucleotide from steps aa) and ab) in an orientation determined by a blockage of ends of the oligonucleotides from steps aa) and ab) that are not to be ligated(See Fig. 2A-3E for example and Col. 6 lines 35-55).

ad) removing oligonucleotides from steps aa), ab) and ac) that are not coupled or ligated(Col. 20 lines 51-57) in a wash with TE(pH 8.0).

ae) cleaving the ligation product from step ac) with a type IIS restriction enzyme which cleaves outside its recognition sequence whereby the cleavage occurs in the nucleic acid sequence of the oligonucleotide from step ab) and resulting in an elongated oligonucleotide and a shorter oligonucleotide(Col. 13, 14, and Fig. 2B) in the reference’s teaching of the “target polynucleotides cleaved with the nuclease of the stepping adaptor may be ligated to a further set of cleavage adaptors A4, A5, and A6 which may contain nuclease recognition sites that are same or different than those contained in cleavage adaptors A1, A2, and A3”(Col. 14 lines40-45).

af) separating the type IIS restriction enzyme and the shorter oligonucleotide reaction mixture from the elongated oligonucleotide obtained in step ae) in their teaching in Col. 22 lines 20-21 that following cleave the beads are washed 3 times in TE (ph 8.0).

ag) repeating steps ab) to af) at least once is taught throughout the reference and specifically in DuBridge’s claim 4 teaching that the process be “repeated one or more times”(Col. 25 and claim 4).

b) providing an oligonucleotide which is prepared by the following steps:

Art Unit: 1634

ba) coupling one end of an oligonucleotide to a solid matrix(Col.19 lines 1-60) wherein the coupling is effected by means of a modification such as highly crosslinked polystyrene beads providing bead-polynucleotide conjugates(Col. 19 lines 65-67 and Col. 20 line 3) and the polynucleotide contains a recognition sequence for a type IIS restriction enzyme(Col. 11 lines 28-37 for example) which cleaves outside its recognition sequence. The reference teaches that “prior to ligation, ends of polynucleotides to be analyzed are prepared by digesting them with one or more restriction endonucleases that produce predetermined cleavages, usually having 3’ or 5’ protruding strands”(Col. 6 lines 21-25).

bb) adding an additional oligonucleotide(Col. 13 and 14 any one of A1, A2, A3 or the “stepping adaptor” references) separate from the oligonucleotide of ba) which is at least partially double stranded(col. 3 line 26 for example) and contains a different recognition sequence than in step ba) for a type IIS restriction enzyme which cleaves outside its recognition sequence, whereby this oligonucleotide cannot bind the matrix, in their teaching of “many target polynucleotides in parallel” and “attaching a first oligonucleotide tag from a repertoire of tags to each polynucleotide in a population of polynucleotides” and “further sampling the population of polynucleotides such that substantially all different polynucleotides in the population have different first oligonucleotide tags attached”(See Col. 11-12, and figures 2A-3E)

bc) ligating the oligonucleotides from steps aa) and ab) in an orientation determined by a blockage of ends of the oligonucleotides from steps ba) and bb) that are not to be ligated(See Fig. 2A-3E for example and Col. 6 lines 35-55).

bd) removing oligonucleotides from steps ba) and bb) that are not coupled or ligated(Col. 20 lines 51-57) in a wash with TE(pH 8.0).

be) cleaving the ligation product from step bc) with a type IIS restriction enzyme which cleaves outside its recognition sequence whereby the cleavage occurs in the nucleic acid sequence of the oligonucleotide from step bb) and resulting in an elongated oligonucleotide and a shorter oligonucleotide(Col. 13, 14, and Fig. 2B) in the reference's teaching of the "target polynucleotides cleaved with the nuclease of the stepping adaptor may be ligated to a further set of cleavage adaptors A4, A5, and A6 which may contain nuclease recognition sites that are same or different than those contained in cleavage adaptors A1, A2, and A3"(Col. 14 lines40-45).

bf) separating the type IIS restriction enzyme and the shorter oligonucleotide from the elongated oligonucleotide obtained in step be), in their teaching in Col. 22 lines 20-21 that following cleave the beads are washed 3 times in TE (ph 8.0) and as can be seen from Figure 2B.

bg) repeating steps bb) to bf) at least once is taught throughout the reference and specifically in DuBridge's claim 4 teaching that the process be "repeated one or more times"(Col. 25 and claim 4) and removing oligonucleotides that are not coupled or ligated to obtain a ligation product.

c) ligating the oligonucleotide from steps a) and b) in an orientation determined by a blockage of ends of the oligonucleotides from steps a) and b) that are not to be ligated(See Fig. 2A-3E for example and Col. 6 lines 35-55).

d) removing oligonucleotides from steps a), b) and c) that are not coupled or ligated(Col. 20 lines 51-57) in a wash with TE(pH 8.0).

e) cleaving the ligation product from step c) with a type IIS restriction enzyme which cleaves outside its recognition sequence whereby the cleavage occurs in the nucleic acid sequence of the oligonucleotide from step a) or step b)and resulting in an elongated

Art Unit: 1634

oligonucleotide and a shorter oligonucleotide(Col. 13, 14, and Fig. 2B) in the reference's teaching of the "target polynucleotides cleaved with the nuclease of the stepping adaptor may be ligated to a further set of cleavage adaptors A4, A5, and A6 which may contain nuclease recognition sites that are same or different than those contained in cleavage adaptors A1, A2, and A3"(Col. 14 lines40-45).

f) separating and thus removing the shorter oligonucleotide and any other component of the solution(Type IIS enzyme) from the elongated oligonucleotide obtained from step e). in their teaching in Col. 22 lines 20-21 that following cleave the beads are washed 3 times in TE (ph 8.0) further wherein the elongated oligonucleotide is retained in the TE wash.

Regarding claim 22, the art is interpreted to teach this limitation, as the oligonucleotide used in step ab) or bb) is a nucleic acid molecule and the reference teaches repeating the procedure.

Regarding claim 23, the method of claim 21 wherein an exonuclease and/or phosphatase reaction is carried out as step ac), bc), or c) after step ac), bc) or c) is taught throughout but specifically in Col. 20 lines 62-65, "the 5' phosphate is removed by treating the bead mixture with an alkaline phosphatase".

Regarding claim 24, the method of claim 21 wherein the shorter oligonucleotide, the unreacted exonuclease and the unreacted phosphatases of step ac'), bc)' or c)' are removed after the reaction also in Col. 20 lines 55-57 in the washing step with TE.

Regarding claim 25, the method of claim 21 where the recognition sequence and the other part of the recognition sequence for this restriction enzyme is derived from the oligonucleotide from step ab), bb) or b)(Col. 13 and 14 any one of A1, A2, A3 or the "stepping

Art Unit: 1634

adaptor” references) which is at least partially double stranded(col. 3 line 26 for example) and contains a different recognition sequence than in step ba) for a type IIS restriction enzyme which cleaves outside its recognition sequence, whereby this oligonucleotide cannot bind the matrix, in their teaching of “many target polynucleotides in parallel” and “attaching a first oligonucleotide tag from a repertoire of tags to each polynucleotide in a population of polynucleotides” and “further sampling the population of polynucleotides such that substantially all different polynucleotides in the population have different first oligonucleotide tags attached”(See Col. 11-12, and figures 2A-3E).

Regarding claim 26, the method of claim 21 wherein the modification is a biotin residue is taught in Col. 13 line 60, as “a biotin, or like moiety, could be employed to anchor the polynucleotide-encoded adaptor conjugate, as no sorting would be required”.

Regarding claim 27, the method of claim 21 wherein the oligonucleotide from step aa), ba), or a) and/or ab), bb) or b) has a loop.(Col. 16 lines 1-4).

Regarding claims 29, 30, and claim 37, DuBridge teaches the method of claim 21 wherein the solid matrix is a bead(Col. 19 and above) and wherein the matrix comprises commercially available CPG and polystyrene beads(e.g.available from Applied Biosystems, Foster City, CA).

Regarding claims 31 and 32 the method wherein the oligonucleotides are complementary and the overhangs at ends of the oligonucleotides from steps aa), ba), a), ab), bb) and b) to be ligated and the single strand overhangs are 1, 2, 3, 4, or 5 nucleotides long, is taught for example in Figures 2A-3E.

Dubridge et al. do not teach the method of claim 21 step bg) wherein the oligonucleotide linked to the solid support is cleaved through a digest with type IIS restriction enzymes.

However, Church et al. teach replica amplification of nucleic acid arrays wherein “a nuclease recognizing the probe cuts the ligated complex at a site one or more nucleotides from the ligation site along the target polynucleotide leaving an end, usually a protruding strand, capable of participating in the next cycle of ligation and cleavage. An important feature of the nuclease is that its recognition site be separate from its cleavage site. In the course of such cycles of ligation and cleavage, the terminal nucleotides of the target polynucleotide are identified. As stated above, one such category of enzyme is that of type IIs restriction enzymes, which cleave sites up to 20 base pairs remote from their recognition sites; it is contemplated that such enzymes may exist which cleave at distances of up to 30 base pairs from their recognition sites.

Therefore, it would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to combine the method of DuBridge et al. with that of Church et al. for the expected benefit of creating a truncation nucleic acid that would now be “capable of participating in the next cycle of ligation and cleavage”(Col. 19 and 20) in the production of additional DNA fragments.

Response to Arguments:

Applicant's arguments filed 5/4/2005 have been fully considered but they are not persuasive. Applicant asserts that on page 15 of their arguments that first, DuBridge et al. “do not include a step of keeping an elongated oligonucleotide while washing away the shorter oligonucleotide, as claimed by applicant in steps ae), af), be), bf), d) and f) in claim 21”.

Art Unit: 1634

However, applicant should first note that claim 21 does not recite this limitation and as a result the issue of whether or not the DuBridge reference teaches it is irrelevant. Applicant's cite many places in their claims on page 12 of their response that almost teach the limitation that they are arguing, but not completely. It is the examiner's viewpoint that applicant is arguing that the Dubridge et al reference does not teach a limitation wherein the shorter of the two oligonucleotides is removed and the longer, elongated oligonucleotide remains bound to the solid support, i.e. the beads. Applicant has not yet claimed this limitation. As presently amended, claim 21 step f) minimally requires that "the elongated oligonucleotide is retained". The claim does not require the elongated oligonucleotide to be retained in a particular fraction or on a particular medium in the method. As such, the rejection of record is maintained. Applicant should note that limitations in applicant's arguments, specification etc couldn't be read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993).

Next applicant argues that while "DuBridge discloses a repeated cycle of ligation and cleavage somewhat similar to Applicant's method, and uses restriction enzymes as claimed by Applicant, the repeated cycles are used for identification of nucleotides of a target polynucleotide resulting in a shorter oligonucleotide" and that "applicant's claims are directed to creating a larger oligonucleotide". However, Dubridge teaches a method of producing a shorter and elongated nucleotide in Figure 2B for example (the oligo on the left being shorter and the one on the right being longer). Furthermore, while figures 3a-3e illustrate an embodiment for DNA sequencing that does not require cycles of ligation and cleavage, DuBridge's claim 4 teaches that the process be "repeated one or more times" (Col. 25 and claim 4).

It is also maintained that in response to applicant's argument that "DuBridge's adaptors

Art Unit: 1634

are ligated and then attached to the solid support” while “applicant’s method requires at least some oligonucleotides to be attached to a solid matrix before ligation” and that their claims carry an “ordered series of steps”(Pg. 16). However, applicant should note that no such requirement for step ab) or ac) to follow step aa) exists and as a result the art need not teach such a sequentially ordered method. For example, applicant’s step ab) does not require that the additional oligonucleotide of ab) is added to the coupled oligonucleotide of aa) only that the second oligonucleotide contain a different recognition sequence than in step aa) and further only that oligonucleotides are ligated from step aa) and ab) not that the ligation is required to occur only after the coupling to the solid matrix. As a result no requirement for order is had by claim 21 step aa), ab), and ac) and as a result the ligation step may precede the step of attaching the oligo to the solid support. Even arguendo, if applicants claims required the specific order DuBridge’s Example in Col. 20-22, teaches that the “bead-polynucleotide mixture is treated with T4 DNA ligase, as described above to complete the ligation of the adaptors to the target polynucleotide”(Col. 22 lines 14-16), thus teaching coupling to a solid matrix before ligation. It should be noted that the examiner has based her rejection on the claims as presently written and through the application of the Dubridge reference that teaches most elements of the claims and the motivation to practice the method as presently claimed in view of the secondary reference and in view of Dubridge’s provision in Col. 18 lines 64-67, that “clearly, one of ordinary skill in the art could combine features of the embodiments set forth above to design still further embodiments in accordance with the invention, but not expressly set forth above”.

While applicant in “an effort to expedite prosecution” has amended step f) of claim 21 to recite “separating and removing the type IIS restriction enzyme and shorter oligonucleotides

Art Unit: 1634

from the elongated oligonucleotide obtained from step e), wherein the elongated oligonucleotide is retained”, as referred to above, no requirement is recited of where the retention of the elongated oligonucleotide occurs. The elongated oligonucleotide is read as being retained in the TE wash solution considering the broadly claimed limitation.

Regarding the secondary reference, the applicant asserts that “Church does not cure the deficiencies of DuBridge as stated above” and as a result requests the withdrawal of the rejection of claims 21-27, 29-32 and 34 under 35 U.S.C. § 103(a). Church et al. do teach cleaving oligonucleotides linked to a solid support with a type IIS restriction enzyme as can be seen in Cols 19(line 62-67) and 20(lines 1-9 and 24-33). As there are no other specific arguments for the Church reference no further response is provided herein.

Lastly, while applicant on page 14 of their response summarizes their asserted deficiencies in the applicability of the Dubridge et al reference, it should be noted that applicant should amend their claims so that they are limited to encompassing the requirements that are presently being argued(providing basis under 112 1st paragraph is had). While applicant’s assertions are all acknowledged, their claims do not necessarily require the argued limitations.

3. Claim 28 is rejected under 35 U.S.C. 103(a) as being unpatentable over DuBridge et al.(US Patent 5,888,737) in view of Church et al.(US Patent 6,485,944) as applied to claim 21 above and in further view of Lane et al.(US Patent 5,770,365).

While the teachings of DuBridge et al.(US Patent 5,888,737) in view of Church et al.(US Patent 6,485,944) are summarized above, they do not teach the method of claim 21 wherein the

Art Unit: 1634

oligonucleotide from step aa), ba) or a) is coupled via a modification in the loop region to the solid matrix.

However, Lane et al. teach nucleic acid capture moieties that in FIG.1 “illustratively shows the hairpin 10 immobilized to an insoluble support 15 through a spacer moiety 12”(Col. 6 lines 44-57).

Therefore, it would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to combine the method of DuBridge et al. in view of Church et al. and in further view of Lane et al. for the expected benefit of covalently linking “sequences B and D together and positions them (e.g. holds them in sufficiently close proximity) such that a B:D intramolecular duplex can form”(Col. 6 lines 51-54).

Response to Arguments:

Applicant's arguments filed 5/4/2005 have been fully considered but they are not persuasive. As there are no specific arguments for this rejection under 103(a) concerning the Church et al. Lane et al. reference, no response is provided herein.

4. Claim 33 is rejected under 35 U.S.C. 103(a) as being unpatentable over DuBridge et al.(US Patent 5,888,737) in view of Church et al.(US Patent 6,485,944) as applied to claim 21 above and in further view of Israel(US Patent 5,981,190).

While the teachings of DuBridge et al.(US Patent 5,888,737) in view of Church et al.(US Patent 6,485,944) are summarized above, they do not teach the method of claim 21 wherein the various type IIS restriction endonucleases are replaced by ribozymes which cleave in an analogous manner.

Art Unit: 1634

However, Israel teaches the analogous manner of using ribozymes and type IIS restriction enzymes in their teaching of type IIS enzymes followed by the teaching that "other methods for cleaving the sample nucleic acid at predetermined sequences include the use of ribozymes"(Col. 11 lines 7-9).

Therefore, it would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to combine the method of DuBridge et al. in view of Church et al. and in further view of Israel since ribozymes are taught by applicant and by Israel to act in an analogous manner as type IIs restriction enzymes.

Response to Arguments:

Applicant's arguments filed 5/4/2005 have been fully considered but they are not persuasive. As there are no specific arguments for this rejection under 103(a) concerning the Church or Israel et al. references, no response is provided herein.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sally A. Sakelaris whose telephone number is 571-272-0748. The examiner can normally be reached on M-Fri, 9-6:30 1st Friday off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Jones can be reached on 571-272-0745. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.


Art Unit: 1634

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Sally Sakelaris



7/19/05



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